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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/733,621

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EXAMINER

KAM, CHIH MIN

ART UNIT

PAPER NUMBER

1656

DATE MAILED: 05/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 10/733,621	Applicant(s) VARADHACHARY ET AL.	
	Examiner Chih-Min Kam	Art Unit 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 March 2006.  
 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.  
 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,3-22 and 35-38 is/are pending in the application.  
     4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
 6) ☒ Claim(s) 1,3-22 and 35-37 is/are rejected.  
 7) ☒ Claim(s) 38 is/are objected to.  
 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.  
 10) ☒ The drawing(s) filed on 11 December 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☐ All    b) ☐ Some \* c) ☐ None of:  
         1. ☐ Certified copies of the priority documents have been received.  
         2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
         3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

### ***Status of the Claims***

1. Claims 1, 3-22 and 35-38 are pending.

Applicants' amendment filed on March 16, 2006 is acknowledged. Applicants' response has been fully considered. Claim 21 has been amended, and a new claim 38 has been added.

Thus, claims 1, 3-22 and 35-38 are examined.

### **Withdrawn Claim Rejections - 35 USC § 112**

2. The previous rejection of claim 21 under 35 U.S.C. 112, second paragraph, is withdrawn in view of applicant's amendment to the claim, and applicant's response at page 5 of the amendment filed March 16, 2006.

### **Withdrawn Claim Rejections - 35 USC § 102**

3. The previous rejection of claims 1, 3-6, 13 and 18 under 35 U.S.C. 102(b) as anticipated by Mita *et al.* (U.S. Patent 5,561,109), is withdrawn in view of applicant's response at page 6 of the amendment filed March 16, 2006.

### **Withdrawn Claim Rejections - 35 USC § 103**

4. The previous rejection of claims 1, 3-8, 11-13, 15, 20-22 and 35 under 35 U.S.C. 103(a) as being obvious over Wu *et al.* (U. S. Patent 5,712,247), is withdrawn in view of applicant's response at pages 7-8 of the amendment filed March 16, 2006.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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5. Claims 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 6 is indefinite because of the use of the term “wherein said lactoferrin is human or bovine”. The cited term renders the claim indefinite, it is not clear what the term means, e.g., it means that the lactoferrin is human or bovine (e.g., lactoferrin is a protein, which is different from human or bovine, a mammal); or, it means the lactoferrin is from human or bovine.

*Response to Arguments*

Applicants indicate the term refers to lactoferrin derived from human or bovine or recombinant versions of the same (see paragraph [0045]), and one of skill in the art would not be confused as to its meaning (page 5 of the response).

Applicants’ response has been considered, however, the arguments are not persuasive because the claim does not clearly indicate the lactoferrin is from human or bovine, the cited term can be read in two different meanings (see paragraph 6 above), thus, the rejection is maintained.

***Maintained Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002

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do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. Claims 1, 3-6, 11, 15, 16 and 18-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Ando *et al.* (US 2004/0018190, filed on November 22, 2001).

Ando *et al.* teach lactoferrin tablets were produced by mixing 50 mg of lactoferrin powder with lactose, cellulose and carboxymethylcellulose calcium salt in a dry state (Example 7), and enteric lactoferrin tablets were administered to a patient suffering from a recurrence of gastric cancer after a surgical operation and retention of cancerous abdominal fluid (paragraph [0056]). In this case, the abdominal fluid was drawn several times a week to relieve pain, after orally taking enteric lactoferrin tablets (lactoferrin dose: 0.45 g per day) for a week, the abdominal fluid was completely absorbed and eliminated (claims 1, 3, 4, 11, 15, 18 and 19). The reference also indicates lactoferrin can be obtained from bovine milk (paragraphs [0011], [0017]; claim 5 and 6), and enteric lactoferrin tablets can deliver the lactoferrin to the lower digestive tract (the duodenum and small intestine; paragraph [0021]; claim 16). Although the reference does not specifically indicate administration of lactoferrin reduces the production or activity of pro-inflammatory cytokines or enhances the production or activity of some cytokines, since the reference teaches the same method steps, it would be expected that administration of lactoferrin would have produced these effects (claims 20-22).

*Response to Arguments*

Applicants indicate Ando discloses use of lactoferrin to treat "a recurrence of gastric cancer after a surgical operation and retention of cancerous abdominal fluid." In the example cited, the abdominal fluid resulted in pressure induced pain, and the lactoferrin treatment of the abdominal illness ameliorated the abdominal fluid pressure and relieved the pain. However, the patient suffering from a recurrence of gastric cancer after a surgical operation and retention of cancerous abdominal fluid" will not necessarily be in pain from either. Hence, the steps disclosed by Ando cannot anticipate the pending method claims (page 7 of the response).

Applicants' response has been considered, however, the arguments are not persuasive because of the following reasons. Ando teaches use of lactoferrin to treat a patient with a recurrence of gastric cancer after a surgical operation and retention of cancerous abdominal fluid, and the abdominal fluid resulted in pressure induced pain, thus, the patient is a cancer patient having pressure induced pain, and administration of lactoferrin can eliminate the abdominal fluid and relieve the pain, which meet the criteria of the claimed invention. Therefore, the rejection is maintained.

***Maintained Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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8. Claims 1, 3-7 and 11-22 under 35 U.S.C. 103(a) as being obvious over Kruzel *et al.* (US 2003/0096736, filed May 7, 2002).

Kruzel *et al.* teach lactoferrin (LF) tablets containing 95.45 parts dextrose, 2.97 parts bovine LF, and 0.53 parts calcium stearate (a known antacid) or a capsule (25 mg) is made (paragraph [0040]) and can be administered to treat autoimmune conditions such as cancer, where lactoferrin may be human lactoferrin, either natural or recombinant, or bovine milk lactoferrin (paragraphs [0022], [0033], [0034]; claims 1, 4-7, 11, 14). The reference also indicates lactoferrin can be administered enterally (claims 15-17), preferably orally, or parenterally, preferably intravenously (claim 12), in the form of injectable solution, or, as a liposomal formulation such as transdermal patches (claim 13), and a single or twice daily dose of 0.01 mg to 20 mg of lactoferrin per kg of body weight is administered (paragraph [0038]; corresponding to 0.6 mg to 1.2 g per day assuming single dose/day and body weight of 60 kg; claims 18 and 19). Although Kruzel *et al.* do not specifically teach using lactoferrin to treat a subject suffering from pain, the reference suggests the use of the same effective amount of lactoferrin (e.g., 0.6 mg to 1.2 g per day, which is in the range of 1 ng to 100g per day used in the claimed method, see paragraph [0073] of US 2004/0151784 (10/733,621)) in the treatment of cancer patients, thus, it would be obvious that the administration of lactoferrin would inherently provide an improvement in the pain associated with cancer (claims 1 and 3). Although Kruzel *et al.* do not specifically indicate lactoferrin reduces the production or activity of pro-inflammatory cytokines (e.g., TNF- $\alpha$ ), or enhances the production or activity of certain cytokines (e.g., IL-18),

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the reference teaches the same method step (the administration of lactoferrin) as the claimed invention, where the lactoferrin would be expected to produce these effects (claims 20-22).

*Response to Arguments*

Applicants indicate the Examiner cannot, of course, establish a *prima facie* case by a conclusory allegation that "it would be obvious that the administration of lactoferrin would inherently provide an improvement in the pain associated with cancer." The Examiner must provide detailed reasoning for this conclusion. The Examiner supports the motivation argument by citing Kruzel's disclosed use of a dosage of lactoferrin allegedly within the scope pending claims. This is may be a necessary predicate fact for the argument. But this fact alone does not explain how one of skill in the art, reading Kruzel, would deduce a suggestion to treat cancer related pain with lactoferrin (page 8 of the response).

Applicants' response has been considered, however, the arguments are not persuasive because of the following reasons. Kruzel *et al.* teach use of lactoferrin to treat a patient with cancer, it is known that cancer patients suffer from pain, and administration of an effective amount of lactoferrin, which is the same amount of lactoferrin in the claimed method, can reduce the pain in the cancer patient, thus, thus, it would be obvious that the administration of lactoferrin would inherently provide an improvement in the pain associated with cancer. Therefore, the rejection is maintained.

***Maintained Claim Rejections-Obviousness Type Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

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F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1, 3-22 and 35-37 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 and 12 of copending Application No. 10/862,213 (now available as US-PGPub 2005/0019342). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 3-22 and 35-37 in the instant application disclose a method of treating a subject suffering from pain comprising administering to the subject an effective amount of a lactoferrin composition to provide an improvement in pain in the subject, wherein the pain is associated with cancers or surgery; or a method of treating a subject suffering from pain comprising administering to the subject an effective amount of a lactoferrin composition consisting essentially of N-terminal variant to provide an improvement in pain in the subject, where the pain is associated with cancers, disorders of the central nervous system or surgery. This is an obvious variation in view of claims 1-8 and 12 in the copending application which disclose a method of treating cancer comprising administering to a subject a cancer immunotherapy and an adjuvant, wherein said adjuvant is a lactoferrin composition that is administered in an amount sufficient to provide improvement in the cancer in the patient; and the specification discloses the lactoferrin composition comprises lactoferrin or an N-terminal lactoferrin variant (paragraph [0009]), where the N-terminal lactoferrin variant mediates the same biological activity as full-

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length lactoferrin, e.g., stimulating the production of various cytokines (e.g., IL-18) and inhibits the production of various pro-inflammatory cytokines (e.g., TNF- $\alpha$ ), and improves parameters which promote or enhance the well-being of subject with respect to the medical treatment of cancer, e.g., a decrease in pain to the subject that can be attributed to the subject's condition (paragraphs [0043], [0059]); and the lactoferrin composition can be administered orally, parentally or topically, for oral administration, an antacid can be administered in conjunction with the lactoferrin composition (paragraph [0012]). Both the claims of instant application and the claims of the copending application are directed to a method of treating a patient suffering from cancer comprising administering an effective amount of a lactoferrin composition to provide improvement in the cancer of the patient such as the pain associated with cancer. Thus, claims 1, 3-22 and 35-37 in present application and claims 1-8 and 12 in the copending application are obvious variations of a method of treating a patient suffering from cancer comprising administering an effective amount of a lactoferrin composition to provide improvement in the cancer of the patient such as the pain associated with cancer.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicants do not provide any arguments in the response.

10. Claims 1, 3-7, 11-13, 15-17, 20-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 13-17, 24, 28, 42-50 and 73-79 of copending Application No. 10/434,769 (now available as US-PG Pub 2004/0009895). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 3-7, 11-13, 15-17, 20-22 in the instant application

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disclose a method of treating a subject suffering from pain comprising administering to the subject an effective amount of a lactoferrin composition to provide an improvement in pain in the subject, wherein the pain is associated with cancers or surgery. This is an obvious variation in view of claims 1-8, 13-17, 24, 28, 42-50 and 73-79 in the copending application which disclose a method of treating hyperproliferative disease such as cancer comprising administering to a subject a human lactoferrin in an amount sufficient to provide an improvement in the hyperproliferative disease. Both the claims of instant application and the claims of the copending application are directed to a method of treating a patient suffering from cancer comprising administering an effective amount of a lactoferrin composition to provide improvement in the condition. Thus, claims 1, 3-7, 11-13, 15-17, 20-22 in present application and claims 1-8, 13-17, 24, 28, 42-50 and 73-79 in the copending application are obvious variations of a method of treating a patient suffering from cancer comprising administering an effective amount of a lactoferrin composition to provide improvement in the condition of the patient such as the pain associated with cancer.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicants do not provide any arguments in the response.

### ***Claim Objections***

11. Claim 38 is objected to because the claim is dependent from a rejected claim.

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***Conclusion***

12. Claims 1, 3-22 and 35-37 are rejected; and claim 38 is objected to.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.  
Patent Examiner



**CHIH-MIN KAM**  
**PATENT EXAMINER**

CMK

May 18, 2006